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(54) Title: PHOSPHATE TRANSPORT INHIBITORS

(57) Abstract: Novel thiophene compounds, useful for treatment of chronic renal failure and uremic bone disease, are disclosed.

PHOSPHATE TRANSPORT INHIBITORS

FIELD OF THE INVENTION

The present invention involves the treatment of chronic renal failure, uremic bone disease and related diseases by inhibition of phosphate retention by certain thiophenes.

BACKGROUND OF THE INVENTION

When kidneys are injured, the adaptive mechanisms involved in restoring homeostasis can lead to additional injury and an inexorable progression to end stage renal disease (ESRD) (Hostetter et al, Am. J. Physiol. 241:F85-F93 (1981)). ESRD affects more than 270,000 patients in the US. While the use of dialysis and kidney transplantation have dramatically improved the survival rate of patients with ESRD, a number of problems have appeared in these patients which complicates their long term management. Early and major contributors to the morbidity of patients with ESRD are abnormalities in mineral and bone metabolism induced by a progressive loss of renal excretory function. Among other factors, phosphate (Pi) retention has been identified as playing a major role in the progression of renal failure and in the generation of secondary hyperparathyroidism (HPTH) and uremic bone disease.

Evidence implicating a role for Pi retention in the progression of chronic renal failure (CRF) has come mainly from studies on experimental animals. Ibels et al, N. Engl. J. Med. 298:122-126, (1978), first demonstrated in a rat model of CRF that dietary Pi restriction prevented renal functional deterioration as assessed by stabilization or improvement of serum creatinine levels, reduced proteinuria, improved histology and reduced mortality. Similar findings were obtained in a rat model of nephrotoxic serum nephritis (Karlinsky et al, Kidney Int. 17:293-302 (1980)). However, these studies were criticized on the basis that a low Pi diet is associated with decreased food intake and thus protein intake which by itself can reduce the progression of CRF. Therefore, Lumlertgul et al, Kidney Int. 29:658-666, (1986) placed 5/6th nephrectomized rats on a normal Pi diet but gave one group a Pi binder. All rats were pair fed and had similar caloric, protein, carbohydrate, vitamin and mineral intakes. At both 6 and 12 weeks rats ingesting the Pi binder showed a lower protein excretion, lower serum creatinine level, lower renal calcium content and less histologic scarring than rats not receiving the Pi binder. This study demonstrated

unequivocally that dietary Pi restriction can have beneficial effects on the progression of CRF independent of caloric and protein intake in experimental animals.

In addition to the beneficial effects of dietary Pi restriction on the progression of CRF discussed above, evidence has also been found that dietary Pi excess can accelerate the progression of CRF. A number of studies in rat models of CRF (Kleinknecht et al, Kidney Int. 5:534-541, (1979); Haut et al, Kidney Int. 17:722-731, (1980); Gimenez et al, Kidney Int. 22:36-41, (1982)) have shown that diets high in Pi lead to a more rapid deterioration in renal function as assessed by serum creatinine levels and the severity of histologic lesions.

Some evidence also suggests that dietary Pi restriction may slow the progression of CRF in patients. Maschio et al, Kidney Int., 22:371-376, (1982) and Maschio et al, Kidney Int., 24:S 273-S 277, (1983) placed patients with mild or moderate renal insufficiency on diets restricted in protein and Pi for up to 76 months. They found that the rate of decline in renal function was slower in the dietary restricted group than in the control group, especially in patients with mild CRF. Barsotti et al., Kidney Int. 24:S278-S284, (1983) and Barsotti et al., Clin. Nephrol. 21:54-59, (1984) placed CRF patients on either a low protein diet or on a low protein-low Pi diet and found that the rate of decline in renal function slowed after the institution of dietary restrictions in both groups. Importantly, they also observed a slower rate of decline in patients on the low protein-low Pi diet compared to the low protein diet alone. In a study of 4 children placed on a low Pi diet serum creatinine levels were halved during the 6 months on the restricted diet compared with a similar period on a normal diet (McCrory et al, J. Pediatr. 111:410-412, (1987). Furthermore, growth velocity in these children increased significantly on the low Pi diet compared with the control period. Other human studies (Barrientos et al, Electrolyte Metab. 7:127-133, (1982); Ciadrella et al, Nephron 42:196-199, (1986); Gin et al, Metabolism 36:1080-1085, (1987)), mainly of short duration, have failed to observe an effect of Pi restriction on the course of CRF. Nevertheless, the bulk of the animal studies discussed above together with the less well controlled human studies suggest that dietary restriction of Pi is beneficial in slowing the progression of CRF, especially in mild to moderate renal insufficiency.

The mechanism by which Pi excess leads to an increase in the rate of renal failure is unknown. However, most evidence supports an interaction between Pi and cellular Ca^{2+} accumulation. In the failing kidney a rise in the filtered load of Pi together with a reduction in Pi reabsorption secondary to elevated levels of parathyroid hormone (PTH) results in an increase in tubular fluid Pi concentration. This leads to an increased transepithelial flux of Ca^{2+} and elevated cellular Ca^{2+} levels resulting in Ca^{2+}-induced cell injury (Borle et al., Endocrinology 102:1725-1732, (1978). Alternatively, or in addition, calcium-phosphate precipitation may occur resulting in renal calcification and nephrocalcinosis (Lau, K., Kidney Int. 36:918-937, (1989)).

Finally, Shapiro et al., Am . J. Physiol. 258:F183-F188, (1990) suggested that the renal hypermetabolism normally associated with the 5/6th nephrectomized model of CRF in rats may contribute to the progression of CRF in this model. Thus, restriction of dietary Pi reduced renal oxygen consumption by 50 % and reduced intracelluar Pi concentrations without altering the steady state concentration of ATP as assessed by ^{31}P-NMR in this model.

Chronic renal failure (CRF) affects more than 270,000 patients in the US alone and costs an estimated $6.8 billion in annual heath care costs. Early and major contributors to the morbidity of CRF patients are abnormalities in electrolyte and bone metabolism induced by the progressive loss of renal excretory function. Phosphate (Pi) retention has been identified as playing a major role in the progression of CRF and in the development of uremic bone disease.

Studies in the literature have shown that dietary Pi restriction slows the progression of CRF in animal models and in small patient studies; decreases elevated plasma PTH levels in CRF animal models and patients; and increases the circulating levels of 1, 25 $(OH)_2$ vitamin D and intestinal Ca^{2+} absorption.

Thus, inhibition of Pi transport by the gut and kidney is considered beneficial in slowing the progression of CRF and uremic bone disease. Thus, inhibition of Pi transport by the gut and kidney is beneficial in slowing the progression of CRF and uremic bone disease.

Consequently, there exists a need to find an alternative means of reducing phosphate retention, in mammals, in addition to diet restriction of phosphate for the treatment of renal diseases, and uremic bone disease.

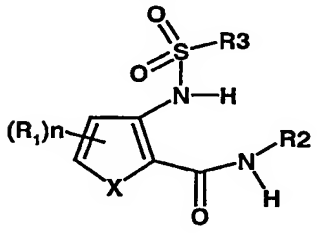
SUMMARY OF THE INVENTION

The present invention involves novel methods of using of thiopenes as phosphate transport inhibitors for the selective inhibition of Pi transport in the kidney and/or the intestine as a therapeutic treatment in chronic renal failure and uremic bone disease.

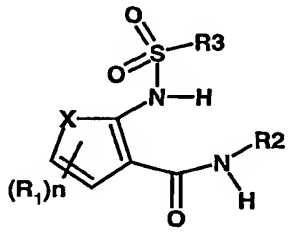
DETAILED DESCRIPTION OF THE INVENTION

The present invention involves the use of inhibitors of phosphate transport, for the treatment of chronic renal failure, and uremic bone disease, as well as other related diseases, such as hyperphosphatemia, vitamin D metabolism, and secondary hyperparathyroidism caused by the retention of phosphate. Preferably, inhibitors for use herein are those which selectively inhibit Na^+-dependent Pi transport in tissues, preferably renal and intestinal tissue, from a number of species, including human.

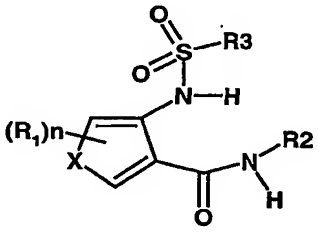
The compounds of the present invention that inhibit phosphate transport are represented by Formulas I, II and III:



I



II



III

X is sulfur or oxygen;

R1 is independently selected from a group consisting of hydrogen, alkyl, aryl, haloalkyl, alkenyl, arylalkyl, arylalkenyl, halo, carboxy, carboalkoxy, carbamyl, alkyl or alkylcarbamyl, cyano, alkoxy, hydroxyl, amino or alkylamino, nitro, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, sulfamyl, aryl or alkylsulfonamido, or represents a fused ring forming a benzothiophene, or (R1)n represents a (R1)n substituted aryl or a heterocycle selected from the group consisting of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole,

imidazole, pyrazole, thiadiazole, oxadiazole, and benzo analogs thereof; or R1 represents a fused ring selected from the group consisting of of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole, imidazole, pyrrazole, thiadiazole, oxadiazole, and benzo analogs thereof,

and

R2 and R3 are not hydrogen, but are independently selected from a group consisting of –(CHR4)n-(CHR5)m-(CHR6)p-(R1 substituted aryl or heteroaryl), alkyl, haloalkyl, or alkyl interrupted by one or more oxygen or sulfur atoms. The carbon chain may also contain a double bond.

m,n, and p are independently 0-3.

R4,R5, and R6 are independently hydrogen, lower alkyl, R1 substituted aryl or heteroaryl,

Preferred compounds include those in which R1 is selected from the group hydrogen, bromide, chloride, methyl, 4-fluorophenyl, 2-thienyl, and

R2 is selected from the group phenyl, 3,5-difluorophenyl, 3-trifluoromethoxyphenyl, 2-methylphenyl, 4-hexyloxyphenyl, 3- or 4-ethoxycarbonylphenyl, 4-benzoylphenyl, 3- or 4-chlorophenyl, 2,3- or 3,4-dichlorophenyl, 3-chloro-4-methoxyphenyl, 4-fluorophenyl, 4-bromophenyl, 4-hexyloxyphenyl, 4-(4-methoxybenzoylaminophenyl), 1-(5-dimethylaminonaphthalene)-yl, 5-isoquinolyl, 6-quinolyl, 6-(2-methylbenzothiazol)-yl, 3-(1,2,4-methylpyrazol)-yl and

R3 is selected from the group phenyl, benzyl, 2-naphthyl, 5-dimethylamin-1-naphthyl, 2-methylphenyl, 3,4-difluorophenyl, 2- or 3-fluorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 2,5-dimethylphenyl, 4-chloro-3,5-dimethylphenyl, 4-nitrophenyl, 4-methoxyphenyl, butyl, octyl, 2,2,2-trifluoroethyl, 2-thiazolyl, 4-(2,1,3-benzothiadiazol)yl, 4-(3,5-dimethylisoxazol)-yl, 3-(2,5-dichlorothiophene)-yl, 5-chloro-2-thienyl, 2-(5-phenylsulfonylthiophene)-yl.

As used herein, "alkyl" refers to an optionally substituted hydrocarbon group joined together by single carbon-carbon bonds. Preferred alkyl substituents are as indicated throughout. The alkyl hydrocarbon group may be linear, branched or cyclic, saturated or unsaturated. All alkyl groups may be substituted with groups

selected from R_3 and the chains may be interrupted at one or more places with hetero atoms such as N, O, or S; the chains may be straight, branched or cyclic; they may be saturated or unsaturated;

As used herein, "aryl" refers to an optionally substituted aromatic group with at least one ring having a conjugated pi-electron system, containing up to two conjugated or fused ring systems. "Aryl" includes carbocyclic aryl, heterocyclic aryl and biaryl groups, all of which may be optionally substituted. Preferred aryl substituents are as indicated throughout.

The compounds of the present invention may contain one or more asymmetric carbon atoms and may exist in racemic and optically active forms. All of these compounds and diastereomers are contemplated to be within the scope of the present invention.

3-Benzenesulfonylamino-N-(3-chlorophenyl)-4-thiophenecarboxamide;

3-Benzenesulfonylamino-N-(3-chlorophenyl)-4-thiophenecarboxamide;

N-(4-Chlorophenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(4-chlorophenyl)-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[(Butylsulfonyl)amino]-N-(4-chlorophenyl)-2-thiophenecarboxamide

3-[(Butylsulfonyl)amino]-N-(3-chloro-4-methoxyphenyl)-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[[(5-Chloro-2-thienyl)sulfonyl]amino]-N-(3,4-dichlorophenyl)-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[(butylsulfonyl)amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[3-(Trifluoromethyl)phenyl]-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamid

3-(2-Fluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(4-Methoxy-benzenesulfonylamino)-thiophene-2-carboxylic acid phenylamide

3-(4-Methoxy-benzenesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(5-Chloro-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(2,2,2-Trifluoro-ethanesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(Butane-1-sulfonylamino)-thiophene-2-carboxylic acid phenylamide

3-(Butane-1-sulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-phenoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hexyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-acetyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzoyl-phenyl)-amide

{4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-phenyl}-acetic acid ethyl ester

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid butyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-propionyl-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(2-hydroxy-ethyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(6-methyl-benzothiazol-2-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-diethylamino-phenyl)-amide

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid 2-diethylamino-ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,4,6-trifluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(1H-indazol-6-ylsulfamoyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(thiazol-2-ylsulfamoyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hydroxymethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-cyclohexyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-fluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid phenylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(pyrimidin-2-ylsulfamoyl)-phenyl]-amide

2-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,6-difluoro-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzo[1,3]dioxol-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-difluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-difluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzoyl-4-chloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [2-(1H-indol-2-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid naphthalen-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (9H-fluoren-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-phenylcarbamoyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methyl-2-oxo-2H-chromen-7-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid biphenyl-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-fluoro-phenyl)-amide

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,6-dimethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloro-pyridin-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-acetyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzoyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-6-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid pyridin-4-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4,6-dimethyl-pyridin-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5,6,7,8-tetrahydro-naphthalen-1-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-pyrrol-1-yl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-indazol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid pyridin-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-fluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (thiophen-2-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid butylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-chloro-pyridin-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dichloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dimethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid phenethyl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-dimethylsulfamoyl-4-methyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-benzotriazol-5-yl)-amide

5-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-2-methoxy-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methyl-benzothiazol-6-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3-dihydro-isobenzofuran-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [3-(1-methyl-1H-pyrazol-3-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [3-(2-methyl-pyrimidin-4-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-oxazol-5-yl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid cyclohexylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-chloro-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-propionic acid ethyl ester

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-butyric acid ethyl ester

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-4-methoxy-benzoic acid methyl ester

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-4-methyl-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-phenylamino-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-8-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-1-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,4,6-trimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5,6-dimethyl-1H-benzoimidazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid indan-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dihydro-benzo[1,4]dioxin-6-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-indol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-dimethylamino-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid #o!-tolylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-benzoimidazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzothiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethanesulfonyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-#tert!-butyl-isoxazol-3-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methyl-pyridin-2-yl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-thiophene-2-carboxylic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzo[1,2,5]thiadiazol-4-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3,5-trimethyl-1H-pyrazol-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4,5-dimethyl-thiazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (furan-2-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,1-dimethyl-propyl)-amide

[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-acetic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-methyl-isoxazol-3-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methoxy-ethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid thiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [1,3,4]thiadiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid biphenyl-3-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(4-chloro-phenoxy)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methylsulfanyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-tetrazol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (thiophen-3-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid naphthalen-1-ylamide

3-[(2-Fluorobenzenesulfonyl)amino]-N-(3,4-difluorophenyl)-2-thiophenecarboxamide

3-[(Butanesulfonyl)amino]-N-(3-trifluoromethylphenyl)-2-thiophenecarboxamide

3-Benzenesulfonyl)amino]-N-(3-chlorophenyl)-4-methyl-2-thiophenecarboxamide

More preferred compounds include, but are not limited to:

3-[(Benzenesulfonyl)amino]-N-(3-chlorophenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(2,3-dichlorophenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(3,5-difluorophenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(4-trifluoromethylphenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(3,4-difluorophenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(2-fluorenyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(3-chloro-2-pyridyl)-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(3-methoxycarbonylphenyl)-2-thiophenecarboxamide

Also preferred compounds include, but are not limited to

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3-dihydrobenzofuran-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-cyclohexylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-chloro-3-methylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-difluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-difluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-fluorophenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-fluorophenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-fluorophenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethoxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hexyloxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-methylenedioxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dimethoxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzyloxyphenyl)- amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methylthiophenyl)- amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methoxyphenyl)- amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropyloxyphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-ethoxycarbonylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxycarbonylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-propionylphenyl)- amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzoylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-(1-keto-1,2,3,4-tetrahydronaphth-7-yl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-acetylphenyl)-amide
3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-acetylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzoyl-4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-methoxycarbonyl-6-methylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethoxycarbonylmethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-(6-methylbenzothiazol-2-yl)phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(2-methylpyrimidin-4-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(oxazol-5-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-5-yl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloropyridin-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(oxazol-5-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-chloropyridin-6-yl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-6-yl-amide

3-Benzene sulfonylamino-thiophene-2-carboxylic acid 1-naphthyl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid 2-thiazolyl amide

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(3-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(4-Trifluoromethoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Chloro-3,5-dimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Bromobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Bistrifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chloro-4-fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Fluoro-6-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3.5-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chloro-2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Chloro-4-fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Bromobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,6-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Iodobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,4-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Nitrobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Acetylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Cyano-2-chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Cyanobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Dichloro-4-hydroxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,5-Dimethoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Methoxy-5-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Difluoro-4-methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,5-Dimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Isopropylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Ethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,4,6-Trimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(1-Naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(5-Dimethylamino-1-naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Dimethyl-4-isoxazolylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,1,3-Benzothiadiazol-4-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(5-Bromothiophene-2-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Chloro-2,1,3-benzo-oxadiazol-7-sulfonylamino)-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(1,3-Dimethyl-5-chloropyrazole-4-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,5-Dichlorothiophene-3-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Methoxycarbonylthiophene-3-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(5-Isoxazol-3-yl-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide

3-(5-Chloro-2,1,3-benzo-oxadiazol-4-sulfonylamino)-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Thienylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(5-Pyridin-2-yl-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide

3-(Butylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Phenylethenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(n-Propylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(i-Propylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(n-Octylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,2,2-Trifluoroethylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-fluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-fluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-trifluoromethoxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-trifluoromethylphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3,5-difluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-n-hexyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-n-butyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3,4-dichlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 2-methylthiophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-benzyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-benzoylphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid phenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 2,3-dichlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-trifluoromethoxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid thiazol-2-yl-amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4,5-dichloro-2-thienyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 5-chloro-2-thienyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 5-phenylsulfonyl-2-thienyl amide

5-(4-Fluorophenyl)-3-(2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

5-(2-Thienyl)-3-(2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

4-Methyl-3-(4-chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-chlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3,5-difluorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3-chlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 2,3-dichlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-fluorophenylamide
4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3-fluorophenylamide
4-(3,4-Difluorobenzenesulfonylamino)-thiophene-3-carboxylic acid 4-fluorophenylamide
2-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-chlorophenylamide
3-Benzenesulfonylaminofuran-2-carboxylic acid 4-isopropylphenylamide
3-Benzenesulfonylaminofuran-2-carboxylic acid 3-chlorophenylamide
3-(3,4-Difluorobenzenesulfonylamino)-furan-2-carboxylic acid 4-fluorophenylamide

Pharmaceutically acceptable salts for use when basic groups are present include acid addition salts such as those containing sulfate, hydrochloride, fumarate, maleate, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, cyclohexylsulfamate and quinate. Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, maleic acid, sulfuric acid, phosphoric acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, *p*-toluenesulfonic acid, cyclohexylsulfamic acid, fumaric acid, and quinic acid.

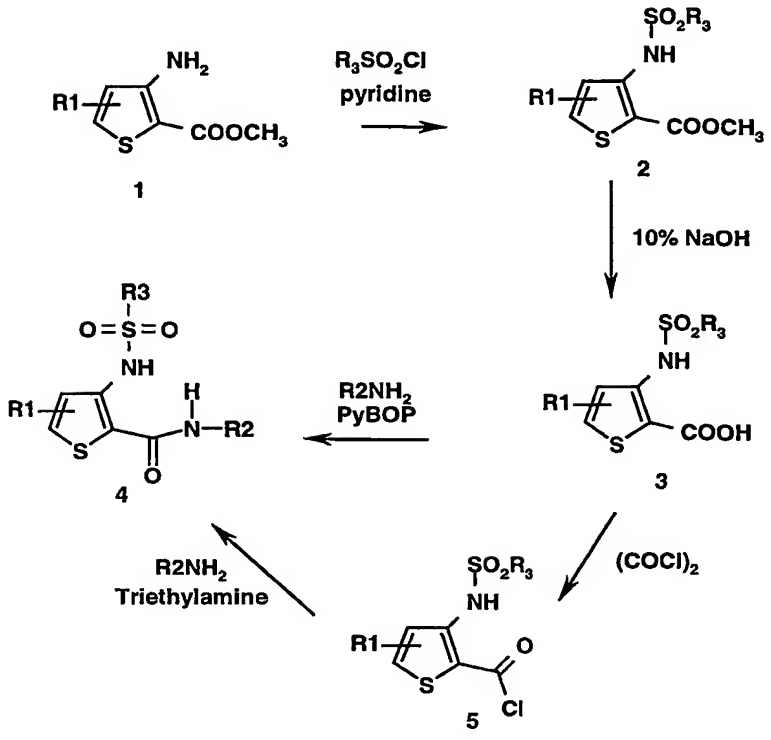
Pharmaceutically acceptable salts also include basic addition salts such as those containing benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine, procaine, aluminum, calcium, lithium, magnesium, potassium, sodium, ammonium, alkylamine, and zinc, when acidic functional groups, such as carboxylic acid or phenol are present.

The present invention provides compounds of Formulas (I) and II above, which can be prepared using standard techniques. An overall strategy for preparing preferred compounds described herein can be carried out as described in this section. Using the protocols described herein as a model, one of ordinary skill in the art can readily produce other compounds of the present invention.

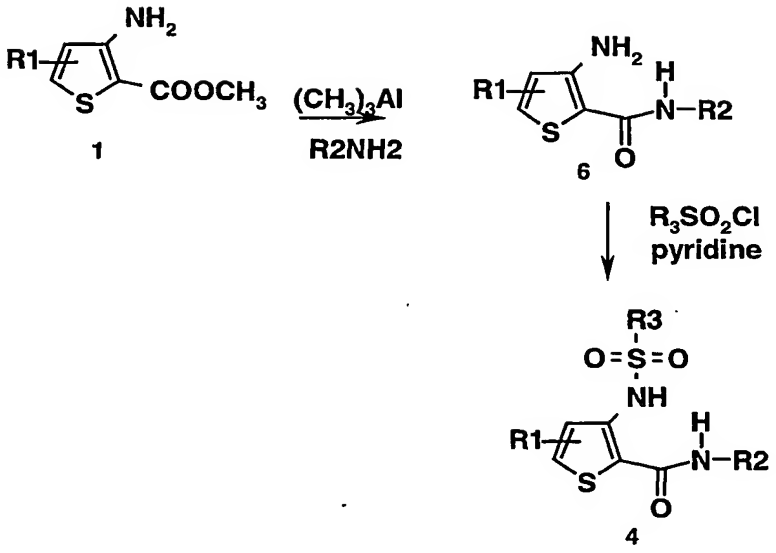
With appropriate manipulation and protection of any chemical functionality, synthesis of the remaining compounds of Formulas (I) and II is accomplished by

methods analogous to those above and to those described in the Experimental section.

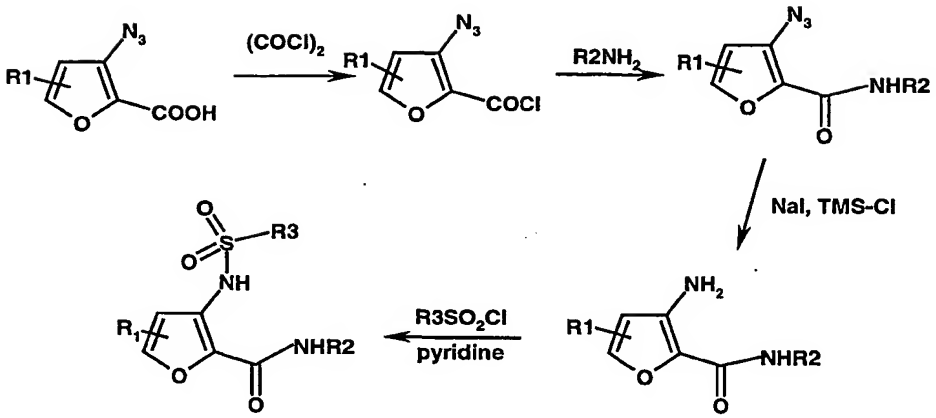
Scheme 1



Scheme 2



Scheme 3



In order to use a present compound or a pharmaceutically acceptable salt thereof for the treatment of humans and other mammals, it is normally formulated in accordance with standard pharmaceutical practice as a pharmaceutical composition.

The present compounds can be administered by different routes including intravenous, intraperitoneal, subcutaneous, intramuscular, oral, topical

(transdermal), or transmucosal administration. For systemic administration, oral administration is preferred. For oral administration, for example, the compounds can be formulated into conventional oral dosage forms such as capsules, tablets, and liquid preparations such as syrups, elixirs, and concentrated drops.

Alternatively, injection (parenteral administration) may be used, *e.g.*, intramuscular, intravenous, intraperitoneal, and subcutaneous. For injection, the compounds of the invention are formulated in liquid solutions, preferably, in physiologically compatible buffers or solutions, such as saline solution, Hank's solution, or Ringer's solution. In addition, the compounds may be formulated in solid form and re-dissolved or suspended immediately prior to use. Lyophilized forms can also be produced.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents may be used to facilitate permeation. Transmucosal administration, for example, may be through nasal sprays, rectal suppositories, or vaginal suppositories.

For topical administration, the compounds of the invention can be formulated into ointments, salves, gels, or creams, as is generally known in the art.

The amounts of various compounds to be administered can be determined by standard procedures taking into account factors such as the compound IC_{50}, EC_{50}, the biological half-life of the compound, the age, size and weight of the patient, and the disease or disorder associated with the patient. The importance of these and other factors to be considered are known to those of ordinary skill in the art.

Amounts administered also depend on the routes of administration and the degree of oral bioavailability. For example, for compounds with low oral bioavailability, relatively higher doses will have to be administered.

Preferably the composition is in unit dosage form. For oral application, for example, a tablet, or capsule may be administered, for nasal application, a metered aerosol dose may be administered, for transdermal application, a topical formulation

or patch may be administered and for transmucosal delivery, a buccal patch may be administered. In each case, dosing is such that the patient may administer a single dose.

Each dosage unit for oral administration contains suitably from 0.01 to 500 mg/Kg, and preferably from 0.1 to 50 mg/Kg, of a compound of Formula (I) or a pharmaceutically acceptable salt thereof, calculated as the free base. The daily dosage for parenteral, nasal, oral inhalation, transmucosal or transdermal routes contains suitably from 0.01 mg to 100 mg/Kg, of a compound of Formula (I). A topical formulation contains suitably 0.01 to 5.0% of a compound of Formula (I). The active ingredient may be administered from 1 to 6 times per day, preferably once, sufficient to exhibit the desired activity, as is readily apparent to one skilled in the art.

As used herein, "treatment" of a disease includes, but is not limited to prevention, retardation and prophylaxis of the disease.

Compositions of present compounds and their pharmaceutically acceptable salts, which are active when given orally, can be formulated as syrups, tablets, capsules and lozenges. A syrup formulation will generally consist of a suspension or solution of the compound or salt in a liquid carrier for example, ethanol, peanut oil. olive oil, glycerine or water with a flavoring or coloring agent. Where the composition is in the form of a tablet, any pharmaceutical carrier routinely used for preparing solid formulations may be used. Examples of such carriers include magnesium stearate, terra alba, talc, gelatin, acacia, stearic acid, starch, lactose and sucrose. Where the composition is in the form of a capsule, any routine encapsulation is suitable, for example using the aforementioned carriers in a hard gelatin capsule shell. Where the composition is in the form of a soft gelatin shell capsule any pharmaceutical carrier routinely used for preparing dispersions or suspensions may be considered, for example aqueous gums, celluloses, silicates or oils, and are incorporated in a soft gelatin capsule shell.

Typical parenteral compositions consist of a solution or suspension of a compound or salt in a sterile aqueous or non-aqueous carrier optionally containing a

parenterally acceptable oil, for example polyethylene glycol, polyvinylpyrrolidone, lecithin, arachis oil or sesame oil.

Typical compositions for inhalation are in the form of a solution, suspension or emulsion that may be administered as a dry powder or in the form of an aerosol using a conventional propellant such as dichlorodifluoromethane or trichlorofluoromethane.

A typical suppository formulation comprises a present compound or a pharmaceutically acceptable salt thereof which is active when administered in this way, with a binding and/or lubricating agent, for example polymeric glycols, gelatins, cocoa-butter or other low melting vegetable waxes or fats or their synthetic analogs.

Typical dermal and transdermal formulations comprise a conventional aqueous or non-aqueous vehicle, for example a cream, ointment, lotion or paste or are in the form of a medicated plaster, patch or membrane.

Preferably the composition is in unit dosage form, for example a tablet, capsule or metered aerosol dose, so that the patient may administer a single dose.

No unacceptable toxological effects are expected when compounds of the present invention are administered in accordance with the present invention.

Sodium-dependent phosphate transport inhibition is determined by the ability of the test compound to inhibit the uptake of radio-labeled inorganic phosphate by proximal tubule cells. Appropriate cells from human, rabbit, or rat may be used.

Phosphate Uptake Assay

Human intestinal cells (I-407, American Type Culture Collection, Manassas, VA, USA) were cultured and harvested according to the supplier's instructions. Rat small intestine epithelial cells were isolated from male Sprague-Dawley rats according to Tepperman et al (Am J Physiol 265:G214-G218, 1993). On the day of the experiment, human intestinal cells were harvested or rat intestinal cells were isolated and washed in uptake buffer at pH 7.4 consisiting of (in mM) NaCl 143; KCl 5.4, $MgCl_2$ 0.8, $CaCl_2$ 1.8, glucose 5 and Hepes 15. Fifty □l aliquots of the

cells (0.5 to 1 million) were distributed in 96-well plates followed by 25 □l of the compound to be tested and 25 □l of 100 □M ^{32}P. The cells were incubated at room temperature for 15 minutes and then isolated by filtration and washed with stop solution which consisted of (in mM) mannitol 100, NaCl 100, Na arsenate 10 and Hepes 5. The cellular uptake of ^{32}P was measured by liquid scintillation counting and expressed either as a per cent of control uptake in the absence of added compounds or as pmol phosphate/ mg cell protein.

In the above noted whole cell assay system for rabbit and human proximal tubule cells the cells are harvested by filtration and ^{32}P uptake is measured. It is also possible to use ^{33}P rather than ^{32}P. Using human proximal tubule cells the IC_{50} for 5-bromo-N-(4-bromophenyl)-2-(5-chloro-2-thienylsulfonamido)benzamide, 5-bromo-N-(4-bromophenyl)-2-(2-fluorophenylsulfonamido)benzamide, and 5-bromo-N-(4-bromophenyl)-2-(3-chloropropylsulfonamido)benzamide are 12, 15, and 14 μM respectively.

The following examples illustrate preparation of compounds and pharmaceutical compositions that may be used in this invention. The examples are not intended to limit the scope of this invention as defined hereinabove and as claimed below.

Example 1

Preparation of N-(4-Fluorophenyl)-3-(phenylsulfonylamino)-thiophene-2-carboxamide

a) **Methyl 3-(Phenylsulfonylamino) thiophene-2-carboxylate**

Methyl 3-aminothiophene-2-carboxylate (10g, 68.6 mmol) was dissolved in 200 ml of pyridine, cooled to 0°, and then benzenesulfonyl chloride (13.8 g, 78.4 mmol) added and the mixture alllowed to warm to 25°C. After one hour a second portion of benzenesulfonyl chloride (13.8 g, 78.4 mmol) was added and the reaction mixture allowed to stand for 20 hours. The reaction mixture was added to a dilute

HCl-ice mixture and the resulting crystals collected by filtration and washed with water to give tan crystals, which after recrystallization from CH_2Cl_2-hexane had mp 109-110°C.

b) **3-Phenylsulfonylaminothiophene-2-carboxylic Acid**

A suspension of 18.8 g (63 mmol) of methyl 3-(phenylsulfonylamino)-thiophene-2-carboxylate in 100 ml of 10% aqueous NaOH was refluxed for two hours and allowed to stand at ambient temperature for 18 hours. The reaction mixture was washed with ethyl acetate and acidified with 10% HCl to give crystals which were collected by filtration and washed with water to give tan crystals, mp 167-169°C.

c) **3-(Phenylsulfonylamino)-2-chlorocarbonylthiophene**

A suspension of 3-phenylsulfonylaminothiophene-2-carboxylic acid (3.8 g, 13.5 mmol) and 1.79 g (14.15 mmol) of oxalyl chloride in 35 ml of CH_2Cl_2 was treated with one drop of DMF and stirred for two hours to give a clear solution. The solution was concentrated in an argon stream and used without further purification in the next reaction.

1R: COCI peak at 1660 cm^{-1}, COOH peak at 1653^{-1} absent.

d) **N-(4-Fluorophenyl)-3-(phenylsulfonylamino) thiophene-2-carboxamide**

A solution of 4-fluoroaniline (0.25 g, 2.25 mmol) and triethylamine (1.52 g, 15 mmol) in 2.5 ml toluene was treated with a toluene - CH_2Cl_2 solution containing 0.53 g (1.77 mmol) of 3-phenylsulfonylamino-2-chlorocarbonylthiophene. After one hour the mixture was filtered and the filtrate dried over $MgS0_4$. Concentration under vacuum gave a gum which was dissolved in DMSO for purification by preparative HPLC: column, OD5-A 30 x 75 mm; gradient 90% H_2O/10% CH_3CN to 10% H_2O/90% CH_3CN (all 0.16 TFA) in 2.7 min. The product, mp 158-160°C, was 100% pure by LC-MS.

A similar procedure using ethyl p-aminobenzoate gave crystals, mp 144-146°C, of **N-(4-ethoxycarbonylphenyl)-3-phenylsulfonylaminothiophene -2-carboxamide**.

Example 2

Preparation of N-(4-Chlorophenyl)-3-(phenylsulfonylamino)thiophene-2-carboxamide

a) **3-Amino-N-(4-chlorophenyl) thiophene-2-carboxamide**

A solution of 4-chloroaniline (6.38 g, 0.05 mmol) was dissolved in 50 ml of toluene, chilled to °C, and treated with 25 ml (0.05 mmol) of 2 M trimethylaluminum in toluene. After 0.5 hour the temperature was allowed to rise to 25°C and held for an additional 0.5 hour at which time no further gas evolution occurred. The reaction mixture was cooled to 0°C and methyl 3-aminothiophene-2-carboxylate added in small portions to control gas evolution. The reaction mixture was allowed to stand at ambient temperatures for 20 hours and then poured carefully to control gas evolution into 250 ml of 10% HCl. The solid which formed was collected by filtration, washed with water and toluene and then dried at 60°C under vacuum. This was used without further purification in the next step.

b) **N-(4-Chlorophenyl)-3-(phenylsulfonylamino)thiophene-2-carboxamide**

A solution of 1.24 g (4.91 mmol) of 3-amino-N-(4-chlorophenyl)-thiophene-2-carboxamide and 1.55 g (19.6 mmol) of pyridine in 50 ml of methylene chloride was treated with 0.9 g (5.15 mmol) of benzenesulfonylchloride and stirred at 25° for 18 hours. The mixture was concentrated under vacuum, and the residue dissolved in ethyl acetate which was then washed in turn with water, 10% aqueous HCl, water, 5% $NaHCO_3$, and then dried over $Mg50_4$. The solution was concentrated under vacuum and the residue dissolved in a minimum of hot ethyl acetate which was then diluted 3-fold with hexane. After standing for 18 hours the crystals which formed were collected, washed with 25% ethyl acetate-hexane, and dried.

Anal. Calcd for $C_{17}H_{13}ClN_2O_3S_2$: C, 51.97; H, 3.34; N, 7.13. Found: C, 51.91; H, 3.23; N, 7.06.

Example 3

Preparation of N-(4-chlorophenyl)-4-methyl-3-(phenylsulfonamido)-thiophene-2-carboxamide

Reaction of methyl 3-amino-4-methylthiophene-2-carboxylate with the complex prepared by reaction of 4-chloroaniline with trimethyl aluminum by the procedure of Example 2 gave 3-amino-N-(4-chlorophenyl)-4-methylthiophene-2-carboxamide as a tan solid. MS: M+1 Calcd, 267; Found, 267. Reaction of this with benzenesulfonyl chloride by the method of Example 2 gave the desired product which after recrystallization from methanol was obtained as colorless crystals. MS: M+1 Calcd 407; Found,
407.

Example 4

Preparation of N-(4-chlorophenyl)-4-(phenylsulfonamido)-thiophene-3-carboxamide

Reaction of methyl 4-aminothiophene-3-carboxylate with the complex prepared by reaction of 4-chloroaniline with trimethyl aluminum by the procedure of Example 2 gave 4-amino-N-(4-chlorophenyl)-3-carboxamide as a tan solid. MS: M+1 Calcd, 267; Found, 267. Reaction of this with benzenesulfonyl chloride by the method of Example 2 gave the desired product which after preparative LC (C-18 ODS, 5 uM particle size, 20 x 50 mm column, 10% acetonitrile-water to 98% acetonitrile (all with 0.1% TFA) 6 min gradient) was obtained as an off-white solid. MS: M+1 Calcd 393; Found, 393. Anal. Calcd for $C_{17}H_{13}ClN_2O_3S_2$: C, 51.97, H, 3.34, N, 7.13. Found: C,51.63, H, 3.30, N,7.24.

Example 5

Parallel Synthesis of N-Substituted-(3-phenylsulfonylamino)-thiophene-2-carboxamides

A 0.53 mmol sample of each amine or amine hydrochloride suspended in 20 ml of toluene containing 0.217 g (2.14 mmol) triethylamine and 0.5 ml of a methylene chloride solution containing 0.064 g (0.20 mmol) of 3-

(phenylsulfonylamino)-2-chlorocarbonylthiophene was added and the mixture stirred 66 hr at amibient temperature. Each reaction vessel was then treated with 3 ml of 10% aqueous HCl, stirred, and filtered. If appreciable crystalline material was collected it was saved for purification. For most sample the toluene filtrate was filtered through several grams of silica gel 60, 230-400 mesh, and the silica gel washed with 5 ml of 10% methanol-chloroform. The combined filtrates were concentrated under vacuum and the residue dissolved in 700 □l of dimethylsulfoxide and purified by preparation HPLC (C18, 20-95% acetonitrile-0.1% acqueous TFA). The products gave satisfactory HPLC-MS analyses.

Example 6

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-fluorophenyl Amide

Methyl N-(3,4-difluorophenylsulfonyl)-3-aminothiophene-2-carboxylate

A solution of 1.73 g (11.03 mmol) of methyl 3-aminothiophene-2-carboxylate in 50 ml of pyridine at 0° C was treated with 4.69g (22.06 mmol) of 3,4-difluorobenzenesulfonylchloride in several portions. After stirring for 18 hr at ambient temperature the reacation mixture was poured into 250 ml of 10% HCl and extracted with ethyl acetate. The organic layer was separated, washed wisth brine, and dried over $MgSO_4$. Concentration under vacuum gave an oil. TLC (silica, $CHCl_3$) product R_f 0.57, starting material, 0.35.

N-(3,4-Difluorophenylsulfonyl)-3-aminothiophene-2-carboxylic Acid

A suspension of about 3.7 g (11 mmol) of methyl N-(3,4-difluorophenylsulfonyl)-3-aminothiophene-2-carboxylate in a mixture of 30 ml of 10% aqueous NaOH, 5 ml of ethanol, and 5 ml of water was refluxed for 4 hr to give a clear amber solution. This was poured into 100 ml of 10% HCl to give a gum which was extracted with ethyl acetate which was washed with brine, dried over $MgSO_4$ and concentrated under vacuum to give a solid. Recrystallization from an

ethanol–water mixture gave tan needles, MP 177-178° C. C,H, and N elemental analysis was satisfactory.

N-(3,4-Difluorophenylsulfonyl)-3-aminothiophene-2-carboxylic Acid Chloride

A suspension of N-(3,4-difluorophenylsulfonyl)-3-aminothiophene-2-carboxylic acid (1.71g, 5.36 mmol) in 14 ml of methylene chloride was treated with 0.71 g (5.63 mmol) of oxalyl chloride and 1 drop of DMF. After 1 hr this reaction mixture was used without further manipulation in the next reaction.

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-fluorophenyl Amide

This compound was prepared as one member of a parallel synthesis array . 4-Fluoroaniline (58.3 mg, 0.52 mmol) was dissolved in 2.5 ml of a solution prepared by dissolving 30 ml of triethylamine in 200 ml of toluene. To this was added at ambient temperature 500 ul of the acid chloride solution and the mixture stirred for 1hr, then an additional 100 ul of acid chloride solution added. The reaction mixture was stirred for 18 hr under a nitrogen atmosphere, and then 725 mg of Combisorb S sulfonic acid scavenger (Agilent, silica gel support, 0.45 mmol per g) added and the mixture stirred for 4 hr. The mixture was then stirred with 2 successive portions of a chloroform-methanol (9:1) solution for 3 hours each. The combined extracts were concentrated under vacuum, and the residue dissolved in about 7 ml of a chloroform-methanol (9:1) solution and then filtered through a 0.45 um frit. After concentration the residue was dissolved in 125 ul of DMSO and a 20 ul portion analyzed by LCMS which indicated the presence of the desired product. The remaining solution was purified by preparative HPLC (C18, 20-95% aqueous acetonitrile, 0.1% TFA in all eluents). The fractions containing product were concentrated under vacuum and analyzed by LCMS. The product was essentially one substance, and had the correct molecular weight.

Example 7

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-n-butyloxyphenyl amide

A solution of 3-(3,4-difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid (63.8 mg, 0.20 mmol) in 1 ml of methylene chloride was treated in turn with diisopropylethylamine (105 ul, 0.6 mmol) and PyBOP (benzotriazol-1-yloxytris(pyrrolidino)phosphonium hexafluorophosphate, 127 mg, 0.24 mmol) and was stirred under argon for 30 min to give a clear solution. Then 36.3 mg (0.22 mmol) of 4-butoxyaniline dissolved in 1 ml of methylenechloride was added. After stirring at ambient temperature for 18 hours the solvent was removed by evaporation under a stream of argon and a sample taken for LCMS. This showed that the expected product was present. The residue was purified by preparative HPLC as in Example 1. LCMS was satisfactory for the purified sample.

Example 8

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-Aminothiophene-2-carboxylic acid 3-chlorphenyl amide

A solution of 10.0 g (78.4 mmol) of 3-chloroaniline in 100 ml of toluene under argon was treated with trimethyl aluminum (39.2 ml, 78.4 mmol of a 2.0 M solution in toluene) in small portions over 30 min. The reaction mixture was stirred for 2.5 hr at ambient temperature and then 12.3 g (78.4 mmol) of methyl 3-aminothiophene-2-carboxylate added in small portions over 5 min. The reaction mixture was stirred at ambient for 18 hr and poured into vigorously stirred 500 ml of 10% HCl. The toluene layer on partial evaporation gave crystals, mp 201-212° C whose NMR spectrum was consistent with the expected structure.

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

A mixture of 3-aminothiophene-2-carboxylic acid 3-chlorphenyl amide (1.06 g, 4.2 mmol), 3-trifluoromethylbenzenesulfonyl chloride, and 0.9 ml of pyridine in 30 ml of methylenechloride was stirred at ambient temperature for 3 hr. The reaction mixture was poured into 10% HCl, the organic phase collected and concentrated under vacuum to give a gum which on trituration with hexane, and then hexane-methylenechloride 2:1 gave crystals, mp 164-165° C, TLC (silica, $CHCl_3$) R_f 0.15-0.25.

Example 9

3-Benzenesulfonylaminofuran-2-carboxylic acid 4-isopropylphenylamide

3-Azidofuran-2-carboxylic acid 4-isopropyphenylamide

3-Azidofuran-2-carboxylic acid was prepared by the method of S. Gronowitz, C. Westerlund and A.-B. Hornfeldt, Acta Chemica Scandinavia B, **29** 224-232 (1975. Oxalyl chloride (71 ul, 0.82 mmol) was added to a suspension of 100 mg (0.65 mmol) of 3-azidofuran-2-carboxylic acid in 50 ml of dichloromethane and 5 ul of DMF. After 1 hr the solvents were removed under a stream of argon, the residue taken up in 50 ml of dichloromethane, and again the solvents removed under a stream of argon. The acid chloride was dissolved in 1 ml of dichloromethane and added to a solution of 0.112 ml (0.816 mmol) of 4-isopropylaniline in 1 ml of pyridine. After 18 hr the solvents were evaporated under a stream of argon and the residue treated with 3 ml of 10% HCl.. On stirring a solid was obtained which had the expected NMR spectrum and correct molecular weight by LCMS.

3-Aminofuran-2-carboxylic acid 4-isopropyphenylamide Hydrochloride

The azide was dissolved in 5.5 ml of acetonitrile and sodium iodide (0.206 g, 1.38 mmol) was added. Then a solution of 0.129 ml of trimethylsilylchloride dissolved in 1.1 ml of acetonitrile was added and the mixture stirred for 18 hr at

ambient temperature. A solution of 10% sodium thiosulfate was then added and the mixture extracted twice with ether. The organic layer was washed in turn with water, brine and then dried over magnesium sulfate. Concentration under vacuum gave a syrup which was dissolved in ether and acidified with ethereal hydrogen chloride to give a solid which was collected and washed with ether, mp 160° C dec.with the correct LCMS and NMR spectrum.

3-Aminofuran-2-carboxylic acid 3-chlorophenylamide hydrochloride prepared in a similar manner had mp 155° C.

3-Benzenesulfonylaminofuran-2-carboxylic acid 4-isopropylphenylamide
Benzenesulfonyl chloride (0.040 ml, 0.31 mmol) was added to a stirred solution of 3-aminofuran-2-carboxylic acid 4-isopropyphenylamide hydrochloride in 0.5 ml of pyridine. After 62 hr the mixture was treated with 2 ml of 10% HCl and the mixture extracted with ethyl acetate. The organic layer was washed in turn with 10% HCl, water, saturated sodium bicarbonate, and brine, and dried over magnesium sulfate. Concentration gave a gum which was purified by preparative HPLC (C18, 20-95% aqueous acetonitrile, 0.1% TFA in all eluents). TLC (silica, hexane-ethyl acetate 6:4) R_f 0.45.

3-Benzenesulfonylaminofuran-2-carboxylic acid 3-chlorophenylamide prepared in a similar manner had R_f 0.29.

Example 10

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3,5-Difluorphenylamide

Methyl 4-Benzenesulfonylamino-thiophene-3-carboxylate

The method of Example 1 was used to obtain crystals, after recrystallization from methylene chloride-hexane, mp 93-95° C, which had the expected values for C, H, and N elemental analysis.

4-Benzenesulfonylamino-thiophene-3-carboxylic Acid

The method of Example 1 was used to obtain crystals, mp 213-215° C, which on TLC (silica, chloroform-methanol 9:1 with a drop of formic acid) had R_f 0.31.

Methyl 4-Benzenesulfonylamino-thiophene-3-carboxylate

The method of Example 1 was used to obtain 4-benzenesulfonylamino-thiophene-3-carboxylic acid chloride, which was used without purification. The acid chloride was dissolved in methylene chloride to give a solution containing 60 mg (0.2 mmol) in 0.5 ml.

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3,5-Difluorphenylamide

3,5-Difluoroaniline (25.8 mg, 0.20 mmol) was added to a suspension of 320 mg of Combisorb S Tertiary Amine Scavenger Resin (silica gel based, 0.8 mmol base per gram) in 2 ml of toluene in tubes fitted with a frit at the bottom. The acid chloride solution (0.5 ml) was added and the mixture shaken under argon for 18 hr. Then 225 mg of Combisorb S Sulfonic Acid Scavenger Resin (silica gel based, 0.45 mmol of acid per gram) was added, the volume adjusted with toluene to 4 ml, and the mixture shaken for 2.5 hr. The toluene solution was collected, and the residue extracted twice with a methylene chloride-methanol mixture. The combined solutions were concentrated under vacuum, the residue dissolved in 0.5 ml of DMSO, and purified by preparative HPLC (C18, 20-95% aqueous acetonitrile, 0.1% TFA in all eluents). The product showed the correct molecular weight by LCMS.

Example 11

2-Benzenesulfonylaminothiophene-3-carboxylic acid 4-Chlorophenylamide

Methyl 2-benzenesulfonylaminothiophene-3-carboxylate was prepared by the method of Example1 for the analogous compound starting from methyl 2-aminothiophene-3-carboxylate (K. Gewald,Chem.Ber. 98, 3571-3577 (1965)). This was converted by the method of Example 1 to 2-benzenesulfonylaminothiophene-3-

carboxylic acid, which had the expected NMR spectrum. This in turn was converted by the method of Example 2 to 2-benzenesulfonylaminothiophene-3-carboxylic acid 4-chlorophenylamide and was purified by preparative HPLC (C18, 20-95% aqueous acetonitrile, 0.1% TFA in all eluents). The product showed the correct molecular weight by LCMS and gave the expected NMR spectrum.

Other compounds useful in the present invention can readily be synthesized using the following amines to prepare carboxamides:

2,6-dimethylaniline
3,4-dimethoxyaniline
4-amino-3,5-dichloropyridine
6-amino-1,2,3,4-tetrahydronaphthalen- 1-one
3-aminoacetophenone
3-aminobenzophenone
6-aminoquinoline
4-aminopyridine
2-amino-4,6-dimethylpyridine
3-benzyloxyaniline
1-amino-5,6,7,8-tetrahydronaphthalene
3,5-dimethoxyaniline
1-(2-aminophenyl)pyrrole
5-aminoindazole
2-aminopyridine
2-fluoroaniline
2-thiophenemethylamine
benzylamine
butylamine
2-amino-5-chloropyridine
2-amino-2-thiazoline
3,4-dimethoxyaniline
4-ethylaniline

2,3-dichloroanilline

2,3-dimethylaniline

2,3-dimethoxyaniline

phenethylamine

3-amino-6-methyl-n,n-dimethylbenzenesulfonamide

5-aminobenzotriazole

methyl 5-amino-2-methoxybenzoate

6-amino-2-methylbenzothiazole

1,3-dihydro-isobenzofuran-5-ylamine

3-(3-aminophenyl)-1-methyl-1h-pyrazole

4-(3-aminophenyl)-2-methylpyrimidine

3-(1,3-oxazol-5-yl)aniline

5-aminoquinoline

cyclohexylamine hydrochloride

2-chloroaniline

beta-alanine ethyl ester hydrochloride

ethyl 4-aminobutyrate hydrochloride

methyl 3-amino-4-methoxybenzoate

methyl 3-amino-4-methylbenzoate

4-n-butylaniline4-butoxyaniline

4-isopropylaniline

4-phenoxyaniline

4-aminobiphenyl

p-hexyloxyaniline

p-anisidine

4-isopropoxyaniline

4-aminoacetophenone

4-aminobenzophenone

ethyl 4-aminophenylacetate

butyl 4-aminobenzoate

p-aminopropiophenone

ethyl 3-aminobenzoate
4-aminophenethyl alcohol
2-(4-aminophenyl)-6-methylbenzothiazole
n,n-diethylphenylenediamine
procaine hcl
2,4,6-trifluoroaniline
n1-(6-indazolyl)sulfanilamide
sulfathiazole
4-morpholinoaniline
4-aminobenzyl alcohol
4-cyclohexylaniline
4-benzyloxyaniline hydrochloride
3-fluoroaniline
3-aminobenzotrifluoride
2-aminobenzotrifluoride
aniline
sulfadiazine
3,4-dichloroaniline
4-chloroaniline
ethyl anthranilate
4-aminobenzotrifluoride
2,6-difluoroaniline
methyl 3-aminobenzoate
3-chloroaniline
2,3-dimethylaniline
3,4-methylenedioxyaniline
2-aminodiphenylamine
3,5-difluoroaniline
3,4-difluoroaniline
2-amino-5-chlorobenzophenone
2-(2-aminophenyl)indole

5-aminoisoquinoline
2-naphthylamine
2-aminofluorene
p-aminobenzanilide
7-amino-4-methylcoumarin
2-aminobiphenyl
4-fluoroaniline; and
benzocaine.

The following sulfonyl chlorides can be used to prepare sulfonamides useful in the present invention:

benzenesulfonyl chloride
3-trifluoromethylbenzenesulfonyl chloride
2-trifluoromethylbenzenesulfonyl chloride
4-trifluoromethylbenzenesulfonyl chloride
3,5-ditrifluoromethylbenzenesulfonyl chloride
2-chlorobenzenesulfonyl chloride
3-chlorobenzenesulfonyl chloride
2-fluoromethylbenzenesulfonyl chloride
3-fluorobenzenesulfonyl chloride
4-fluorobenzenesulfonyl chloride
3,4-difluorobenzenesulfonyl chloride
3,5-difluorobenzenesulfonyl chloride
4-trifluoromethoxybenzenesulfonyl chloride
4-chloro-3,5-dimethylbenzenesulfonyl chloride
4-bromobenzenesulfonyl chloride
4-bromo-2,5-difluorobenzenesulfonyl chloride
3-chloro-4-fluorobenzenesulfonyl chloride
4-acetylbenzenesulfonyl chloride
2-chloro-4-cyanobenzenesulfonyl chloride
4-cyanobenzenesulfonyl chloride
4-nitrobenzenesulfonyl chloride

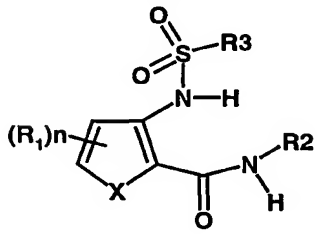
4-methoxybenzenesulfonyl chloride
3,4-dimethoxybenzenesulfonyl chloride
3,5-dichloro-4-hydroxybenzenesulfonyl chloride
2,5-dimethoxybenzenesulfonyl chloride
3-methoxybenzenesulfonyl chloride
2-methoxy-5-methylbenzenesulfonyl chloride
2-methylbenzenesulfonyl chloride
2,5-dimethylbenzenesulfonyl chloride
4-isopropylbenzenesulfonyl chloride
4-methylbenzenesulfonyl chloride
4-ethylbenzenesulfonyl chloride
2,4,6-trimethylbenzenesulfonyl chloride
2-naphthylsulfonyl chloride
5-dimethylamino-1-naphthylsulfonyl chloride
3,5-dimethyl-4-isoxazolylsulfonyl chloride
2,1,3-benzthiadiazol-4-ylsulfonyl chloride
5-bromo-2-thienylsulfonyl chloride
2,1,3-benzoxadiazol-7-chloro-4-ylsulfonyl chloride
5-chloro-1,3-dimethyl-4-pyrazolylsulfonyl chloride
2,5-dichloro-3-thienylsulfonyl chloride
2-ethoxycarbonyl-3-thienylsulfonyl chloride
5-(3-oxazolyl)-2-thienylsulfonyl chloride
2-thienylsulfonyl chloride
1-butylsulfonyl chloride
1-propylsulfonyl chloride
2-propylsulfonyl chloride
1-octylsulfonyl chloride
2,2,2-trifluoroethylsulfonyl chloride
2-phenylvinylsulfonyl chloride

All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

The above description fully discloses the invention including preferred embodiments thereof. Modifications and improvements of the embodiments specifically disclosed herein are within the scope of the following claims. Without further elaboration, it is believed that one skilled in the area can, using the preceding description, utilize the present invention to its fullest extent. Therefore the Examples herein are to be construed as merely illustrative and not a limitation of the scope of the present invention in any way. The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows.

What is claimed is:

1. A compound according to Formula I, Formula II or Formula III:



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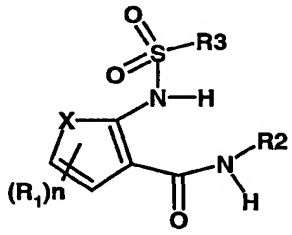

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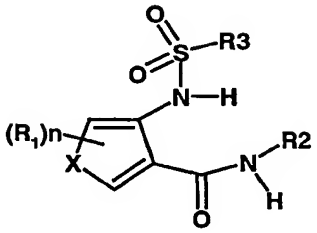

III

wherein

X is sulfur or oxygen;

R_1 is independently selected from a group consisting of hydrogen, alkyl, aryl, haloalkyl, alkenyl, arylalkyl, arylalkenyl, halo, carboxy, carboalkoxy, carbamyl, alkyl or alkylcarbamyl, cyano, alkoxy, hydroxyl, amino or alkylamino, nitro, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, sulfamyl, aryl or alkylsulfonamido, or represents a fused ring forming a benzothiophene, or $(R_1)n$ represents a $(R_1)n$ substituted aryl or a heterocycle selected from the group consisting of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole, imidazole, pyrazole, thiadiazole, oxadiazole, and benzo analogs thereof; or R_1 represents a fused ring selected from the group consisting of thiophene, furan, pyridine, pyrimidine, pyrazine, isoxazole, thiazole, imidazole, pyrrazole, thiadiazole, oxadiazole, and benzo analogs thereof,

and

R2 and R3 are not hydrogen, but are independently selected from a group consisting of –(CHR4)n-(CHR5)m-(CHR6)p-(R_1 substituted aryl or heteroaryl), alkyl, haloalkyl, or alkyl interrupted by one or more oxygen or sulfur atoms. The carbon chain may also contain a double bond.

m, n, and p are independently 0-3.

R4,R5, and R6 are independently hydrogen, lower alkyl, R_1 substituted aryl or heteroaryl,

2. A compound according to Claim 1 wherein R_1 is selected from the group consisting of hydrogen, bromide, chloride, methyl, 4-fluorophenyl, and 2-thienyl, and

R2 is selected from the group consisting of phenyl, 3,5-difluorophenyl, 3-trifluoromethoxyphenyl, 2-methylphenyl, 4-hexyloxyphenyl, 3- or 4-ethoxycarbonylphenyl, 4-benzoylphenyl, 3- or 4-chlorophenyl, 2,3- or 3,4-dichlorophenyl, 3-chloro-4-methoxyphenyl, 4-fluorophenyl, 4-bromophenyl, 4-hexyloxyphenyl, 4-(4-methoxybenzoylaminophenyl), 1-(5-dimethylaminonaphthalene)-yl, 5-isoquinolyl, 6-quinolyl, 6-(2-methylbenzothiazol)-yl, and 3-(1,2,4-methylpyrazol)-yl and

R3 is selected from the group consisting of phenyl, benzyl, 2-naphthyl, 5-dimethylamin-1-naphthyl, 2-methylphenyl, 3,4-difluorophenyl, 2- or 3-fluorophenyl, 4-chlorophenyl, 3-trifluoromethylphenyl, 2,5-dimethylphenyl, 4-chloro-3,5-dimethylphenyl, 4-nitrophenyl, 4-methoxyphenyl, butyl, octyl, 2,2,2-trifluoroethyl, 2-thiazolyl, 4-(2,1,3-benzothiadiazol)yl, 4-(3,5-dimethylisoxazol)-yl, 3-(2,5-dichlorothiophene)-yl, 5-chloro-2-thienyl, and 2-(5-phenylsulfonylthiophene)-yl.

3. A compound according to Claim 1 wherein the compound is selected from the group of:

3-Benzenesulfonylamino-N-(3-chlorophenyl)-4-thiophenecarboxamide;

3-Benzenesulfonylamino-N-(3-chlorophenyl)-4-thiophenecarboxamide;

N-(4-Chlorophenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[(Benzenesulfonyl)amino]-N-(4-chlorophenyl)-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(4-Chlorophenyl)-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[(Butylsulfonyl)amino]-N-(4-chlorophenyl)-2-thiophenecarboxamide

3-[(Butylsulfonyl)amino]-N-(3-chloro-4-methoxyphenyl)-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-(3,4-Dichlorophenyl)-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

3-[[(5-Chloro-2-thienyl)sulfonyl]amino]-N-(3,4-dichlorophenyl)-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[1,1'-Biphenyl]-4-yl-3-[(butylsulfonyl)amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(2-fluorophenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(4-methoxyphenyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[(phenylsulfonyl)amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(5-chloro-2-thienyl)sulfonyl]amino]-2-thiophenecarboxamide

N-(3-Chloro-4-methoxyphenyl)-3-[[(2,2,2-trifluoroethyl)sulfonyl]amino]-2-thiophenecarboxamide

N-[3-(Trifluoromethyl)phenyl]-3-[[[3-(trifluoromethyl)phenyl]sulfonyl]amino]-2-thiophenecarboxamid

3-(2-Fluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(4-Methoxy-benzenesulfonylamino)-thiophene-2-carboxylic acid phenylamide

3-(4-Methoxy-benzenesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(5-Chloro-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(2,2,2-Trifluoro-ethanesulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-(Butane-1-sulfonylamino)-thiophene-2-carboxylic acid phenylamide

3-(Butane-1-sulfonylamino)-thiophene-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-phenoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hexyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-acetyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzoyl-phenyl)-amide

{4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-phenyl}-acetic acid ethyl ester

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid butyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-propionyl-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(2-hydroxy-ethyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(6-methyl-benzothiazol-2-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-diethylamino-phenyl)-amide

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid 2-diethylamino-ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,4,6-trifluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(1H-indazol-6-ylsulfamoyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(thiazol-2-ylsulfamoyl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hydroxymethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-cyclohexyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-fluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid phenylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(pyrimidin-2-ylsulfamoyl)-phenyl]-amide

2-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,6-difluoro-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzo[1,3]dioxol-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-difluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-difluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzoyl-4-chloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [2-(1H-indol-2-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid naphthalen-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (9H-fluoren-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-phenylcarbamoyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methyl-2-oxo-2H-chromen-7-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid biphenyl-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-fluoro-phenyl)-amide

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-benzoic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,6-dimethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloro-pyridin-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-acetyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzoyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-6-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid pyridin-4-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4,6-dimethyl-pyridin-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzyloxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5,6,7,8-tetrahydro-naphthalen-1-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-pyrrol-1-yl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-indazol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid pyridin-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-fluoro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (thiophen-2-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid butylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-chloro-pyridin-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dichloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dimethyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid phenethyl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-dimethylsulfamoyl-4-methyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-benzotriazol-5-yl)-amide

5-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-2-methoxy-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methyl-benzothiazol-6-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3-dihydro-isobenzofuran-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [3-(1-methyl-1H-pyrazol-3-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [3-(2-methyl-pyrimidin-4-yl)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-oxazol-5-yl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid cyclohexylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-chloro-phenyl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-propionic acid ethyl ester

4-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-butyric acid ethyl ester

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-4-methoxy-benzoic acid methyl ester

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-4-methyl-benzoic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-phenylamino-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-8-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-1-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,4,6-trimethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5,6-dimethyl-1H-benzoimidazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid indan-5-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dihydro-benzo[1,4]dioxin-6-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-indol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-dimethylamino-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid #o!-tolylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-benzoimidazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzothiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethanesulfonyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethoxy-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-#tert!-butyl-isoxazol-3-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methyl-pyridin-2-yl)-amide

3-[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-thiophene-2-carboxylic acid methyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid benzo[1,2,5]thiadiazol-4-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloro-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3,5-trimethyl-1H-pyrazol-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4,5-dimethyl-thiazol-2-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (furan-2-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,1-dimethyl-propyl)-amide

[(3-Benzenesulfonylamino-thiophene-2-carbonyl)-amino]-acetic acid ethyl ester

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (5-methyl-isoxazol-3-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methoxy-ethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid thiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [1,3,4]thiadiazol-2-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid biphenyl-3-ylamide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid [4-(4-chloro-phenoxy)-phenyl]-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methylsulfanyl-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1H-tetrazol-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (thiophen-3-ylmethyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid naphthalen-1-ylamide

3-[(2-Fluorobenzenesulfonyl)amino]-N-(3,4-difluorophenyl)-2-thiophenecarboxamide

3-[(Butanesulfonyl)amino]-N-(3-trifluoromethylphenyl)-2-thiophenecarboxamide

3-Benzenesulfonyl)amino]-N-(3-chlorophenyl)-4-methyl-2-thiophenecarboxamide

4. A compound according to claim 1 selected from the group consisting of:

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (1,3-dihydrobenzofuran-5-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-cyclohexylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2,3-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-dichloro phenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-chloro-3-methylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-difluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-difluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-fluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-fluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-fluorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-trifluoromethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-trifluoromethoxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-hexyloxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,4-methylenedioxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dimethoxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-benzyloxyphenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-methylthiophenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-methoxyphenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-isopropyloxyphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-ethoxycarbonylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-butoxycarbonylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-propionylphenyl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-benzoylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-(1-keto-1,2,3,4-tetrahydronaphth-7-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-acetylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-acetylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (2-benzoyl-4-chlorophenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-methoxycarbonyl-6-methylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-ethoxycarbonylmethylphenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (4-(6-methylbenzothiazol-2-yl)phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(2-methylpyrimidin-4-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(oxazol-5-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid isoquinolin-5-yl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3,5-dichloropyridin-4-yl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-(oxazol-5-yl)-phenyl)-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid (3-chloropyridin-6-yl)- amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid quinolin-6-yl-amide

3-Benzene sulfonylamino-thiophene-2-carboxylic acid 1-naphthyl-amide

3-Benzenesulfonylamino-thiophene-2-carboxylic acid 2-thiazolyl amide

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(3-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(4-Trifluoromethoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Chloro-3,5-dimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Bromobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Trifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Bistrifluoromethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chloro-4-fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Fluoro-6-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3.5-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Chloro-2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Chloro-4-fluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Bromobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,6-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Iodobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,4-Dichlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Nitrobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Acetylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Cyano-2-chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Cyanobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Dichloro-4-hydroxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,5-Dimethoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3-Methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Methoxy-5-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,5-Difluoro-4-methoxybenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,5-Dimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Isopropylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(4-Ethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,4,6-Trimethylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2-Naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(1-Naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(5-Dimethylamino-1-naphthylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(3,5-Dimethyl-4-isoxazolylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(2,1,3-Benzothiadiazol-4-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(5-Bromothiophene-2-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(4-Chloro-2,1,3-benzo-oxadiazol-7-sulfonylamino)-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(1,3-Dimethyl-5-chloropyrazole-4-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(2,5-Dichlorothiophene-3-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(2-Methoxycarbonylthiophene-3-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(5-Isoxazol-3-yl-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide
3-(5-Chloro-2,1,3-benzo-oxadiazol-4-sulfonylamino)-sulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(2-Thienylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(5-Pyridin-2-yl-thiophene-2-sulfonylamino)-thiophene-2-carboxylic acid (3-chloro-phenyl)-amide
3-(Butylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(2-Phenylethenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(n-Propylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(i-Propylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide
3-(n-Octylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(2,2,2-Trifluoroethylsulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-fluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-fluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-trifluoromethoxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-trifluoromethylphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3,5-difluorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-n-hexyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-n-butyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-chlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3,4-dichlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 2-methylthiophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-benzyloxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-benzoylphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid phenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 2,3-dichlorophenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4-trifluoromethoxyphenyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid thiazol-2-yl-amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 4,5-dichloro-2-thienyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 5-chloro-2-thienyl amide

3-(3,4-Difluorobenzenesulfonylamino)-thiophene-2-carboxylic acid 5-phenylsulfonyl-2-thienyl amide

5-(4-Fluorophenyl)-3-(2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

5-(2-Thienyl)-3-(2-methylbenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

4-Methyl-3-(4-chlorobenzenesulfonylamino)-thiophene-2-carboxylic acid 3-chlorophenyl amide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-chlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3,5-difluorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3-chlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 2,3-dichlorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-fluorophenylamide

4-Benzenesulfonylamino-thiophene-3-carboxylic acid 3-fluorophenylamide

4-(3,4-Difluorobenzenesulfonylamino)-thiophene-3-carboxylic acid 4-fluorophenylamide

2-Benzenesulfonylamino-thiophene-3-carboxylic acid 4-chlorophenylamide

3-Benzenesulfonylaminofuran-2-carboxylic acid 4-isopropylphenylamide

3-Benzenesulfonylaminofuran-2-carboxylic acid 3-chlorophenylamide

3-(3,4-Difluorobenzenesulfonylamino)-furan-2-carboxylic acid 4-fluorophenylamide

5. A method of causing phosphate excretion and/or inhibiting phosphate absorption by administering to a subject in need thereof a safe and effective amount of a compound according to claim 1.

6. A method of treating chronic renal failure by inhibiting the phosphate transport system in a mammal in need thereof, by administering to a subject in need thereof a safe and effective amount of a compound a compound according to claim1.

7. A method according to claim 6 wherein uremic bone disease is treated.

8. A method according to claim 6 wherein the phosphate transport is inhibited in the kidney.

9. A method according to claim 6 wherein the phosphate transport is inhibited in the intestine.

10. A method of inhibiting sodium dependent phosphate transport by administering to a subject in need thereof a safe and effective amount of a compound according to claim 1.

11. A method of inhibiting oxidative phosphorylation in a subject in need thereof comprising administering a safe and effective amount of a compound according to claim 1.

12. A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.